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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
| 001444-166 | 02/20/97 | CAMPBELL | R CAMPBELL-2A |

001444 HM22/0114
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| EXAMINER | |
| SPECTOR, L | |
| ART UNIT | PAPER NUMBER |
| 1646 | 22 |

DATE MAILED: 01/14/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- Responsive to communication(s) filed on 10/5/99
- This action is FINAL.
- Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- Claim(s) 1-14, 19 is/are pending in the application.
Of the above, claim(s) 7-13 remain ~~is/are~~ withdrawn from consideration.
- Claim(s) _____ is/are allowed.
- Claim(s) 1-6, 14, 19 is/are rejected.
- Claim(s) _____ is/are objected to.
- Claim(s) 1-14, 19 were ~~is/are~~ subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been
- received.
- received in Application No. (Series Code/Serial Number) _____
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- Notice of Reference Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

Part III: Detailed Office Action

The request filed on 10/27/99 for a Continued Prosecution Application (CPA) under 37 C.F.R. § 1.53(d) based on parent application number 08/804166 is acceptable and a CPA has been established. An action on the CPA follows.

5 The amendment filed 10/5/99 has been entered. Claims 1-6, 14 and 19 are pending and under consideration. Claims 7-13 remain withdrawn from prosecution as being drawn to non-elected species.

10 The rejection of claims 1-5, 14 and 19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of applicant's amendments .

15 The rejection of claims 1, 2, 3, 5, 14 and 19 under 35 U.S.C. 102(b) as being anticipated by Johnson et al., Biol. Reprod. 52:68, reference AC cited by applicants is withdrawn in view of applicant's amendments .

20 The rejection of claims 1-5, 14 and 19 under 35 U.S.C. 103(a) as being unpatentable over Capon et al., U.S. Patent number 5,116,964, in view of Fiddes et al., references BR and BS, cited by applicants (Nature 281:351 and 286:684) is withdrawn in view of applicant's amendments .

Applicants arguments filed 10/5/99 have been fully considered but are not deemed persuasive for reasons below:

20

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

25 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 14 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention.

Claim 1 is indefinite for reciting "an antibody light chain which is associated with a corresponding antibody heavy chain, and an antibody heavy chain which is associated with a corresponding antibody light chain", because it is not clear in what manner the chains are 'associated',
5 and further because it is not clear what the final structure would be or look like; it would appear that a light chain which is associated with a heavy chain *already* is a heterodimer, such that it is not clear how that heterodimer could *further* be 'dimerized' by association of part (b) of the molecule with another part (b) of another molecule, to *form* a heterodimer.

Claim 1 is also indefinite as the preamble states that the hybrid protein is a 'heterodimer',
10 whereas the conclusion of the claim states that the sequences 'dimerize and form a heterodimer complex'. It is not clear what the difference is between a 'heterodimer' and a 'heterodimer complex'.

Claim 2 is indefinite for reciting 'antibody light (or heavy) chains or fragments thereof optionally associated with the respective heavy (or light) chains'. First, it would appear that moiety
15 (a) of claim 1 should be singular, thus recitation of the plural 'antibody light (or heavy) chains' is indefinite. Second, the claim is not further limiting of claim 1 with respect to the recitation of 'optionally', as the association with the cognate chain (heavy to light or light to heavy) is now required by claim 1.

Claim 14 remains indefinite as it is not clear how the "one or more non-native interchain disulfide bonds" are added. It is not clear from the claim whether applicants intend to induce non-native bonds between native cysteines, or alternatively are trying to indicate that additional cysteines
20 have been introduced into the subunits for the purpose of forming such bonds.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

25 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 14 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is not commensurate in scope with claims wherein portion (a) is an antibody or other protein that is in and of itself dimeric in nature. As stated in the above rejection under 35 U.S.C. §112, second paragraph, and using an antibody as an exemplary species, such an antibody would already be a dimer. It is noted that claim 1 includes the limitation that the protein dimerizes by aggregation of portions (b) of the fusion protein. The specification has not taught how to promote dimerization preferentially through portion (b) of the molecule in those species wherein portion (a) is additionally capable of dimerization. In those instances in which either end of the recited protein is capable of dimerization, it is not predictable which end would predominate, nor how to control such. It would seem that such would be dependent upon the respective kinetics of the two possible dimerization events, and that in some instances, both might be able to occur. Given the unpredictability and lack of guidance, the examiner concludes that it would require undue experimentation to determine how to assure that dimerization would occur via the (b) moiety.

15

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

20

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 14 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Boime, U.S. Patent number 5,705,478 for reasons cited in the Office Action mailed 5/22/98, at page(s) 4-5.

Applicants arguments submitted 10/5/99, paper number 16, have been fully considered but
5 are not deemed persuasive. Applicants argue that due to the amendment of part (a) of claim 1 to exclude gonadotropins, that the rejection must fall. This argument has been fully considered but is not deemed persuasive because while this addresses point (B) raised by the Examiner in paper number 13 at page 5, points (A) and (C) therein remain valid, and the rejection is maintained on those bases.

10 **Advisory Information:**

No claim is allowed. Claim 6 would be allowable if amended to overcome the above rejections under 35 U.S.C. §112.

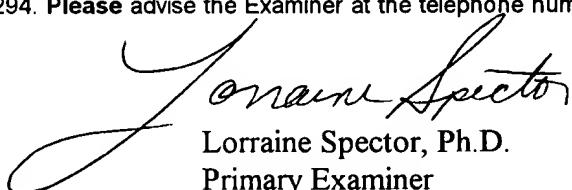
15 Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, Ph.D., can be reached at (703)308-4623.

20 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

25 Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

30 Official papers filed by fax should be directed to (703) 305-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Please advise the Examiner at the telephone number above when an informal fax is being transmitted.



Lorraine Spector
Primary Examiner

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